

Serial No. 08/455,975

Page 46, line 39, delete "II-3" and insert --Rubin et al., Proc. Natl. Acad. Sci. USA 86: 802-806 (1989)--.

Page 61, line 13, delete "II-3" and insert --Rubin et al., Proc. Natl. Acad. Sci. USA 86: 802-806 (1989)--.

Page 65, delete lines 1-23.

IN THE ABSTRACT:

Please delete the present Abstract (at page 52 of the Substitute Specification) and substitute therefor the following:

--

ABSTRACT

Isolated Keratinocyte Growth Factor (KGF) having preferential mitogenic activity on cells of epithelial origin is described. Methods of treating a condition by specific stimulation or inhibition of epithelial cell growth using KGF also are described. --

A copy of the new Abstract is attached for the Examiner's convenience.

IN THE FIGURES:

Amended Figures 1-10 are attached hereto.

IN THE CLAIMS:

Please delete claim 22, without prejudice or disclaimer. Please amend the claims as follows:

21. (amended) A method of treating a condition[s] by [requiring] specific stimulation of epithelial cell[s] growth comprising administering to a

*C1
Conclusion*

patient having the condition, an epithelial cell growth stimulating amount of [substantially pure human] Keratinocyte Growth Factor (KGF) polypeptide, or portion thereof having preferential mitogenic activity on cells of epithelial origin [that is characterized by], wherein said polypeptide has a molecular weight between 16 and 30 kDa [and a specific activity of at least about 3.4 x 10⁴ units per milligram of protein].

CJ

23. (amended) A method of treating a condition by specific stimulation of epithelial cell growth comprising administering to a patient having the condition, an epithelial cell growth stimulating amount of Keratinocyte Growth Factor (KGF) polypeptide, [according to Claim 22] wherein the KGF polypeptide comprises the amino acid sequence presented in Figure [II-1B] 7, [wherein the N-terminus is cysteine 32 and the C-terminus is threonine 194] or portion thereof.

24. (amended) A method according to claim 21 wherein the polypeptide, or portion thereof is administered [as] in a pharmaceutical composition further comprising [human] KGF as presented in Figure II-1B wherein the N-terminus is cystein 32 and the C-terminus is threonine 194 and] an acceptable pharmaceutical carrier.

25. (amended) A method of treating a condition[s] [requiring] by specific stimulation of epithelial cell[s] growth comprising administering to a patient having the condition, an epithelial cell growth stimulating amount of a [substantially pure chimeric]

(D)
cont.

Keratinocyte Growth Factor (KGF) polypeptide having preferential mitogenic activity on cells of epithelial origin, wherein said [chimeric] polypeptide comprises [a functional domain of human KGF and a polypeptide of a different member of the fibroblast growth factor (FGF) family] amino acids 32-78 of Figure 7 or a portion thereof fused to the coding sequence of a member of the fibroblast growth factor (FGF) family that is not KGF, wherein the coding sequence corresponds to amino acids 79-194 of Figure 7.

26. (amended) A method of accelerating or improving [wound] the healing of a wound involving [the epidermis,] tissue of epithelial origin, the method comprising administering to the wound site, an epithelial cell growth stimulating amount of a pharmaceutical composition comprising:

(a) a [substantially pure human] Keratinocyte Growth Factor (KGF) polypeptide, or portion thereof having preferential mitogenic activity on cells of epithelial origin, wherein said polypeptide has [characterized by] a molecular weight between 16 and 30 kDa [and a specific activity of at least about 3.4×10^4 units per milligram of protein]; and

(b) an acceptable pharmaceutical carrier.

27. (amended) A method of treating a condition[s] [requiring] by specific inhibition of epithelial cell[s] growth, the method comprising administering to a patient having said condition, an epithelial cell growth inhibiting amount of a pharmaceutical composition, wherein

*C1
C2
C3
Completed*

said pharmaceutical composition comprises (a) an isolated antibody that binds [against] a Keratinocyte Growth Factor (KGF) polypeptide having preferential mitogenic activity on cells of epithelial origin and [selected from the group consisting of a polypeptide comprising a unique portion of an amino acid sequence s presented in Figure II-1B wherein the N-terminus is cysteine 32 and the C-terminus is threonine 194, and a polypeptide comprising an allelic variant of human KGF] comprising the amino acid sequence of Figure 7, or a portion thereof and (b) a pharmaceutically acceptable carrier.

28. (amended) A method of stimulating epithelial cell growth in vitro comprising adding an amount of [substantially pure human] Keratinocyte Growth Factor (KGF) polypeptide, or portion thereof having preferential mitogenic activity on cells of epithelial origin to a culture comprising epithelial cells, the amount of the polypeptide, or portion thereof, being sufficient to stimulate epithelial cell growth, wherein said KGF polypeptide [is characterized by] has a molecular weight between 16 and 30 kDa [and has a specific activity of at least about 3.4×10^4 units per milligram of protein].

Please enter the following new claims:

C3

-- 30. A method according to claim 23 wherein the polypeptide or portion thereof is administered in a pharmaceutical composition further comprising an acceptable pharmaceutical carrier.

31. The method of any one of claims 21, 23, 24, 26, 27, 28 or 30, wherein said KGF polypeptide comprises amino acids 65-156 and 162-189 of Figure 7.

(C3) 32. The method of any one of claims 21, 23, 24, 26, 27, 28 or 30, wherein said KGF polypeptide is encoded by a DNA molecule selected from the group consisting of:

(a) a cDNA molecule comprising the DNA sequence of Figure 7;

(b) a cDNA molecule comprising the polypeptide coding region in Figure 7;

(c) a cDNA molecule as defined in (b) further comprising a 5' ATG;

(d) a human DNA molecule which encodes an mRNA that hybridizes to the 695-bp *Bam*HI/*Bc*II cDNA fragment as set forth in Figures 6 and 7, under conditions wherein such *Bam*HI/*Bc*II fragment hybridizes to a 2.4 kb KGF mRNA transcript expressed in a M426 cell line, but not to human aFGF or human bFGF mRNA transcripts in RNA samples from cell lines which express such transcripts; and

(e) a DNA molecule which is degenerate from and encodes a polypeptide encoded by the DNA molecule defined in one of (a) - (d).

33. The method of any one of claims 21, 23, 24, 26, 27, 28 or 30, wherein said KGF polypeptide is truncated within the region encoding amino acids 32-78 of the sequence of Figure 7.

34. The method of any one of claims 21 or 23-30, wherein said KGF polypeptide shows preferential mitogenic

activity for BALB/MK epithelial cells, but not NIH/3T3 fibroblast cells.

35. The method of any claim 31, wherein said KGF polypeptide shows preferential mitogenic activity for BALB/MK epithelial cells, but not NIH/3T3 fibroblast cells.

*C3
Cen/Chw*

36. The method of any claim 32, wherein said KGF polypeptide shows preferential mitogenic activity for BALB/MK epithelial cells, but not NIH/3T3 fibroblast cells.

37. The method of any claim 33, wherein said KGF polypeptide shows preferential mitogenic activity for BALB/MK epithelial cells, but not NIH/3T3 fibroblast cells.--

REMARKS

Claims 21-29 are pending in this application. Claim 22 is herewith deleted without prejudice or disclaimer and claims 30-37 are added. Thus, with the entry of this amendment, claims 21 and 23-37 will be active in this case.

I. **MISCELLANEOUS**

Examiner Saoud has requested that the priority information be updated, that the title be amended and that the Figures, Tables and Description of the Figures be corrected. The Examiner also has objected to the abstract. Finally, the Examiner has requested applicants to correct errors made in the Preliminary Amendment filed